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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,363	11/17/2003	Edgardo Laborde	25352-0032D1	6673

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HELLER EHRMAN WHITE & MCAULIFFE LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 02/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,363	LABORDE ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-48 and 50-71* is/are rejected.

7)☒ Claim(s) *49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 40-71 are pending. Claims 1-39 have been canceled according to the amendment filed on 9-22-2004.

Election/Restrictions

2. In response to the restriction requirement, Applicant has elected without traverse the invention of Group IV, wherein Y=O and Z=N.

The method claims and the multiple active ingredients composition claims have been amended to the scope of the elected compound of Group IV. The method of use claims and the multiple active ingredients composition claims are therefore rejoined.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 66-68, 70-71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant method of treating an allergic, inflammatory, or autoimmune disorder or disease reaches out to all allergic, inflammatory or autoimmune disorders/diseases not described in the specification and the as yet unidentified allergic, inflammatory or autoimmune disorders/diseases, the description of which is not found in the specification.

A full description of anit-inflammatory drug, cytokine, or immunomodulator is not found in the specification. Furthermore, it reaches out to as yet unidentified anit-inflammatory drug, cytokine, or immunomodulator, a description of which is not found in the specification.

The method of inhibiting leukocyte migration reaches out to as yet unidentified conditions/disorders/diseases, a description of which is not found in the specification.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 71 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims directed to mediating a biological pathway are devoid identifiable utility and are therefore not useful. Unless the pathway at issue is critical to treating some condition and the pathway modification and disease treatment are inexorably linked, such pathway modification is devoid of utility. The instant claim directed to a mechanism of inhibiting leukocyte migration without the end result would therefore have no practical utility unless the inhibition of leukocyte migration and the treatment of a disease are inexorably linked. Since the claims as recited embrace any degree of inhibition of leukocyte migration, which may or may not inexorably linked to the treatment of the disease, the scope of the claims is therefore not commensurate with that of the objective enablement, especially in view of the absence of a full written description of the as yet unidentified conditions/activities/disorders which the recited mechanism reaches out to. One of ordinary skill in the art therefore would not be able to use the inventive compound as claimed without undue experimentation.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-48, 50-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compound of formula A, Aa, B, or Ba wherein R4 and R5 do not form a ring for treating the disorder/disease as recited in claim 69, does not reasonably provide enablement for the method of treating any allergic, inflammatory or autoimmune disorder/disease or for making and using the compound of formula A, Aa, B, or Ba wherein R4 and R5 together form a ring. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

a. *Nature of the invention.*

The instant invention is drawn to bicyclic compound as MCP-1 antagonist and, the composition, the multiple active ingredients composition, and the methods of use thereof.

b. *State of the prior art and the level of the skill in the art.*

MCP-1 is a member of the CC class of chemokines. Its effect is mediated primarily via the CCR2B receptor (Forbes, PTO-1449). Antagonist of MCP-1 have been described (Forbes, PTO-1449; Faull, 6288103; PTO-1449; Kato, WO 97/24325, PTO-1449; Connor, WO 98/06703, PTO-1449), however, the instant compound does not resemble any of these prior art antagonist compounds.

It is well recognized in the art that not all inflammatory, allergic or autoimmune disorders/diseases are mediated by MCP-1.

The level of the skilled in the MCP-1 antagonist art is high.

c. *Predictability/unpredictability of the art.*

The high degree of unpredictability is well recognized in the chemokine receptor antagonist art. A small change in the structure would drastically affect its biological activity as

evidenced in the different K_i values for the structurally similar compounds with only one difference (Forbes, page 11805, Tables 1-4).

d. *Amount of guidance/working examples.*

How to make

The preparation of example compounds is limited to compounds wherein R4 and R5 does not form a ring. Starting materials and the process of making the instantly claimed compounds wherein R4 and R5 together form a ring are not seen but required. Sources are particularly pertinent because absent sources, the public is offered mere language, rather than enablement. Ex parte Moersch 104 USPQ 122. In re Howarthe 210 USPQ 689.

How to use

The procedures for assessing the effects of the example compounds in the inhibition of MCP-1 induced-chemotaxis, in the adjuvant arthritis model in rat, collagen-induced arthritis model in rat, restenosis model in rat, and the anti-thy-1-antibody induced nephritis model, and the results thereof, have been described on pages 82-91 of the specification.

e. *The breadth of the claims.*

Applicant's assertion that all the structurally diverse compounds (including the compounds of formula II, and the compound of formula I wherein R4 and R5 form a ring) would be effective as MCP-1 antagonists and useful for treatment of any inflammatory, allergic or autoimmune disorders/diseases (including those unrelated to MCP-1, and those as yet unidentified inflammatory, allergic or autoimmune disorders/diseases, which are not fully described in the specification) does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability and the working examples limited only to compounds of formula I wherein R4 and R5 does not form a ring (paragraphs b, c, d above).

f. *Quantitation of undue experimentation.*

Since sufficient teaching and guidance have been provided in the disclosure, one of ordinary skill in the art, even with high degree of skill, would not be able to make and use all the compounds as claimed without undue experimentation except for the compounds wherein R4 and R5 do not form a ring for treatment of diseases recited in claim 69.

Allowable Subject Matter

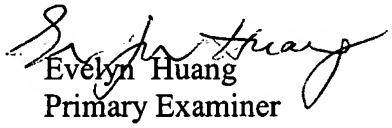
6. Claim 49, wherein R4 and R5 does not form a ring, is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Levin (6228869) discloses a sulfonamido isoxazolo[4,5-b]pyridine carboxylic acid, hydroxyamide compound (column 48, Example 94) which differs from the instant in not having the urea attached to the carbonyl. Motivation to modify the prior art compound to arrive at the instant invention is lacking.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Evelyn Huang
Primary Examiner
Art Unit 1625